

REMARKS

The present claims have not been changed from applicants' prior response. Thus, claims 1-13 and 20 appear in this application.

Applicants appreciate the Examiner's noting that Applicants' response of December 24, 2003 "will overcome the 112 rejection and 102 rejection." Applicants provide the following remarks in order to more completely respond to the prior Office Action as it regards the rejection under 35 U.S.C. §103.

The present invention is directed to retroviral-infected immortalized human keratinocyte or melanocyte cell lines which retain the ability to differentiate and express proteins and enzymes expressed by normal differentiated keratinocytes or melanocytes even after high passage in tissue culture--keratin proteins expressed by normal differentiated keratinocytes or melanin proteins expressed by normal differentiated melanocytes.

As explained in our previous response, Boukamp *et al.* and Steinkraus *et al.* are directed to immortalization of keratinocytes without the use of a retrovirus construct to minimize the virus-related effects on differentiation. The cell lines produced in these references were produced using spontaneous immortalization techniques with no retroviral construct. The references actually teach away from the present invention, teaching that immortalization using retroviral constructs should be avoided in order to obtain normal differentiation.

Neither Boukamp *et al.* nor Steinkraus *et al.* discloses a retroviral-infected immortalized human keratinocyte or melanocyte cell line that retains the ability to differentiate and express proteins and enzymes expressed by normal differentiated keratinocytes or melanocytes even after high passage in tissue culture as expressly required by the claims. Boukamp *et al.* summarizes the prior art by stating that the retroviral produced cell lines resulted in "cells that exhibited altered growth properties and substantial reduction of normal keratinization as well as partial reexpression of fetal characteristics" concluding that the "deficiencies in differentiation are invariably associated with transformation and/or malignancy." Steinkraus *et al.* simply uses the non-retroviral-infected cells produced in Boukamp *et al.*

The Examiner's statement that "keratinocytes and melanocytes, as well as SV40 immortalization methods, were well known at the time of the invention" does not remedy the deficiencies of the cited references. Neither reference discloses the presently claimed cell lines and actually teach away from them. It appears from the references cited by

the Examiner that the presently claimed cell lines were thought not to be possible to produce at the time of the invention. It was Applicants that first discovered and taught a method of obtaining retroviral-infected immortalized human keratinocyte or melanocyte cell lines with the ability to differentiate and express proteins and enzymes expressed by normal differentiated keratinocytes or melanocytes even after high passage in tissue culture. Nothing cited by the Examiner alone or in combination, including the statement that the keratinocytes, melanocytes and SV40 immortalization methods were well known, teaches or suggest the presently claimed invention.

One skilled in the art would not be motivated or enabled to make Applicants' presently claimed retroviral-infected cell line without the inventors' disclosure or the use of hindsight, which is expressly prohibited. Only the inventors' specification teaches one how to produce the presently claimed cell lines that retain the ability to differentiate and express normal proteins and enzymes using a retrovirus. This is further demonstrated by the references cited by the Examiner, which teach away from Applicants invention.

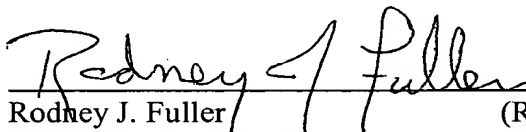
In view of the deficiencies of the cited references and the state of the art at the time of the invention, Applicants respectfully request that this rejection be withdrawn.

In view the foregoing remarks and amendments it is believed that the entire application is now in condition for allowance. Should any issues remain please call Allan Fanucci at (212) 294-3311 or Rodney Fuller at (202) 371-5838 in order to expedite the allowance of all the claims in this application.

Respectfully submitted,

Date

4/1/04



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